November 16, 1893.

Sir JOHN EVANS, K.C.B., D.C.L., LL.D., Vice-President and Treasurer, in the Chair.

Professor Arthur Mason Worthington was admitted into the Society.

A List of the Presents received was laid on the table, and thanks ordered for them.

In pursuance of the Statutes, notice of the ensuing Anniversary Meeting was given from the Chair.

Professor A. H. Church, Sir J. Cockle, and Professor W. C. Roberts-Austen were by ballot elected Auditors of the Treasurer's accounts on the part of the Society.

The following Papers were read :—

I. "On Hepatic Glycogenesis." By D. Noël Paton, M.D., Superintendent of the Research Laboratory of the Royal College of Physicians of Edinburgh. Communicated by Professor McKendrick, F.R.S. Received July 24, 1893.

(Abstract.)

Glycogenesis is here used in its original sense as indicating the whole process of sugar production in the liver.

The origin of sugar in the liver has been so conclusively demonstrated that it is not considered.

The evidence in regard to the relationship of hepatic sugar to hepatic glycogen is discussed, and is considered as conclusively in favour of Bernard's original view.

On the source of glycogen, all subsequent work has but established Bernard's conclusion: "L'acte *vital*, c'est la production du glycogène au sein du tissu vivant."

On the mode of conversion of glycogen to sugar, more recent work has not tended to confirm Bernard's view, that "L'acte *chimique* c'est la transformation du glycogène en sucre." The question of whether this conversion is due to a zymin, as held by Bernard, or to the vital action of the liver protoplasm, as suggested by recent writers, is, as yet, undecided.

The object of the present communication is to elucidate this point,

and the question considered is, how far the process of conversion of glycogen to sugar is dependent or independent of the life of the liver cells.

To determine this, the rate of conversion of glycogen to glucose in the excised liver, roughly minced, and kept at from 37° to 40° C. in normal salt solution, was first investigated. The object of the experiments not being to keep the liver cells alive as long as possible, but to differentiate between changes during the life of the cells and after their death, normal salt solution was used in preference to defibrinated blood.

Instead of estimating the sugar, as in Seegen's and Dalton's experiments, the glycogen was directly determined. For the analyses, the method of Brücke was found more suitable than that of Külz. The sources of error of the method are considered at length.

The following table gives a summary of the results of the experiments upon this subject, and shows that during the first half hour the conversion of glycogen is very rapid, that it steadily diminishes during the remainder of the first hour, and after this goes on very slowly.

No. of experiment.	Time in minutes from commencement.	Loss of glycogen per 100 parts liver.	Loss of glycogen per 100 parts liver per 10 minutes.
5, 1st hour	3	0·25	0·85
1 "	4	0·85	2·05
3 "	10	0·58	0·58
5 "	13	1·21	0·93
2 "	45	0·86	0·19
4 "	60	0·533	0·089
3, 2nd hour	95	0·5	0·05
4, 3rd hour	155	1·49	0·07
1, 4th hour	240	1·66	0·069
4, 5th hour	255	1·205	0·051
2, 6th hour	315	1·67	0·05
4 "	375	1·855	0·049

The relationship of the early rapid and the subsequent slow change of the glycogen to the condition of the liver cells is next considered, under these heads :—

A. Influence of Destruction of the Morphological Structure of the Liver Cells on Hepatic Amylolysis.

The liver of a rabbit, freshly killed and bled, was divided into three. One part, A, was pounded in a mortar with fine clean sand, and was then kept in salt solution at 40° C. The second part, B, roughly minced, was placed in a similar solution. The third part, C, was used to determine the initial amount of glycogen. At the end of some time A and B were boiled, and the glycogen extracted. The following two experiments show that destruction of the structure of the liver cells very greatly inhibits the conversion of glycogen.

A.	B.	C.	Time.
5·48	4·41	5·97	1 hr. 48 m.
5·061	2·336	5·267	4 8

B. Structural Changes in Liver Cells of Excised Liver kept under the Conditions above described.

The histological methods employed are described and the structure of the normal liver cell is considered. In the liver kept in salt solution at 40° C. as above described the protoplasm network becomes more apparent and then breaks up and tends to collect round the nucleus. The nucleus, somewhat later, loses its distinct outline and its network and stains diffusely. Finally, it breaks up.

These changes begin to manifest themselves usually within the first hour, and are often not completed even at the end of twenty-four hours.

The conversion of glycogen seems thus divisible into two periods.

1. An early period of rapid conversion occurring before obvious structural changes appear in the liver cells.
2. A late period of slow conversion after the changes above described have developed.

The rapid and extensive conversion appears to be inhibited by destroying the structure of the liver cells.

Further to elucidate the nature of these changes, the influence of various factors upon them was studied.

I. *Temperature.*—The possibility of distinguishing between zymins and living ferments by the influence of temperature of over 60° C. in destroying the latter, but not the former, is discussed, and it is concluded that it has a distinct, though restricted, value. So far as they go, the following experiments, showing that exposure for one hour to a temperature of 60° C. inhibits, but does not completely stop, hepatic amylolysis,* favour the view that the process is dependent on a living ferment rather than on a zymin.

* "Hepatic amylolysis" is used throughout this paper as an abbreviation fo "the conversion of hepatic glycogen to sugar."

Per cent. of Glycogen in Liver.

Initial glycogen.	Glycogen in part exposed to 60° C. and afterwards to 40° C.	Glycogen in part exposed from first to 40° C.
0·805	0·763	0·200
0·811	0·700	0·450

II. *Fluoride of sodium*, in 1 per cent. solution, according to Arthus and Huber, checks the action of protoplasm, but does not interfere with the activity of zymins. It is shown that it markedly retards hepatic amylolysis. It does not accelerate the structural changes in the liver cells.

III. *Chloroform water*, according to Salkowski, is a reagent which stops the vital action of protoplasms, but does not interfere with the action of zymins.

He gives an experiment upon its influence on hepatic amylolysis, from which he concludes that he has established the accuracy of Bernard's view, that the conversion is due to a zymin. In a series of experiments I have obtained results opposed to that of Salkowski. Three portions of the liver were taken. One (A) was used for the determination of the initial glycogen. The other two parts were placed in separate vessels in normal saline at from 37° to 40° C. Through one of these (B) a stream of chloroform vapour was conducted, a stream of air being directed through the other (C). The following results were obtained :—

A.	B.	C.	Time.
3·459	0·000	0·102	4 hrs.
0·811	0·165	0·450	5
Lost	0·735	1·012	3
2·160	0·841	1·273	4
2·07	0·73	0·97	6

Experiments were also made which show that the glycogen is actually converted to glucose.

Chloroform markedly increases hepatic amylolysis.

To determine whether the early rapid or the latter slow conversion is thus accelerated, the following experiment was performed. In it the large letters indicate the presence of chloroform, the small letters its absence :—

	Glucose.		Glycogen.		Time.
	Glucose per cent.	Gain per 10 min.	Glycogen per cent.	Loss per 10 min.	
Initial .	0·23	—	7·09		
B.....	1·39	0·308	5·68	0·31	45 min.
b	0·98	0·218	6·23	0·19	
C.....	1·96	0·06	5·00	0·07	next 90 min.
c	1·66	0·07	5·60	0·07	
D.....	2·58	0·036	4·60	0·02	next 180 min.
d	1·88	0·012	5·42	0·01	

It is the early rapid amylolysis which is accelerated.

The influence of chloroform upon the structural changes in the liver cells was investigated, and it was found that the disintegrative changes are markedly accelerated, occurring within the first half hour. This may indicate that the rapid early conversion is due to the more rapid katabolic changes in the protoplasm preceding its death.

The occurrence of glycæmia and glycosuria after the administration of chloroform rendered it desirable to ascertain if this accelerated amylolysis occurs in the living animal under the action of the drug. For this purpose, rabbits of one litter were kept on the same diet and daily weighed, in order to approximate the amount of glycogen in their livers. For each experiment a pair of as nearly equal weight as possible were selected. One was lightly anæsthetised for three or four hours, the other was not. The fallacies in this method of experiment are fully considered.

Animal.	Per cent. of glycogen in liver.	
	Check animal.	Chloroformed animal.
Rabbit............	1·437	0·75
,, ...	0·354	0·016
,, ...	3·91	1·664
,, ...	0·665	0·092
Dog.............	1·425	1·103
,, ...	1·000	

Such experiments seem to indicate that during life chloroform accelerates hepatic amylolysis.

IV. *Ether* is found to have the same action on the amylolysis in the excised liver as chloroform, but to a much less marked extent. Its action in bringing about structural changes in the liver cells is also less marked.

V. *Pyrogallic acid*, in 0·25 per cent. neutral solution, acts in the same manner upon the process of amylolysis and upon the liver cells.

VI. *Morphin* (0·005 to 0·025 per cent.), *curare*, *nitrate of amyl* (vapour through salt solution), *and salicylate of soda* (0·5 per cent.), neither increase hepatic amylolysis nor do they accelerate the cellular changes. The glycosuria caused by the administration of the first three of these is not due to increased hepatic amylolysis.

The products of hepatic amylolysis in the early and in the later stage were also investigated. In the early stage, glucose appears to be formed directly, and no intermediate bodies, such as dextrins or maltose, occur. In the later amylolysis, the former of these, possibly the latter, are always found.

In the light of these observations, the nature of the hepatic amylolysis is considered, and it is maintained that the evidence shows that the early rapid amylolysis is different from the later slow process, and that it is simply the result of the katabolic changes in the protoplasm accentuated as death occurs; that it is, in fact, simply an exaggeration of the process of amylolysis during life; and that it is in no way due to the action of a zymin, but is comparable to the production of mucin from mucinogen, and zymin from zymogen.

The later slow amylolysis is next considered. The development of an acid reaction, partly, at least, due to lactic acid, is shown; but experiments are given indicating that the acidity is not the cause of the amylolysis. The influence of micro-organisms is also investigated, and experiments are given to show that the process goes on as rapidly when these are excluded as when they are present. The evidence of the existence of a zymin in the dead liver is considered, and the conclusion is drawn that the later slow amylolysis is due to the action of such a zymin, probably developed during the disintegration of the liver cells.

II. "On certain Correlated Variations in *Carcinus mœnas*." By W. F. R. Weldon, M.A., F.R.S., Fellow of St. John's College, Cambridge, Professor of Zoology in University College, London. Received August 9, 1893.

In previous communications I have discussed the variations in size occurring in one or two organs of the common shrimp (*Crangon vulgaris*). In these papers it has been shown (1) that the observed